R E M A R K S

Obviousness-type double patenting rejection

Claims 25, 26 and 28-34 have been rejected under the judicially created doctrine of obviousness-type double patenting with the assertion that claims 25, 26 and 28-34 are obvious over claims 1-30 of U.S. Pat. No. 5,932,208. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

The Examiner asserts that the presently claimed invention is obvious over the claims of U.S. '208. U.S. '208 discloses the use of muramyl peptides in combination with interferon to potentiate the effects of the interferon. The present invention, on the other hand, is drawn to a method of treatment using muramyl peptides as the principle, i.e. efficacious, ingredient, for inhibiting the replication of acquired immune deficiency.

U.S. '208 claims methods of treating cancer, infections, diseases or genetic deficiencies (claim 17), methods of inducing the granulocyte system in a patient (claim 18), methods for the rapid reconstitution of the haematopoietic system (claim 19) and methods of treating viral diseases (claim 20).

There is no recitation or suggestion in U.S. '208 of treating AIDS. In addition, there is no disclosure or suggestion in U.S. '208 of using muramyl peptides as the principal ingredient for

treating AIDS, or as more specifically recited in the present claims of methods of inhibiting the replication of acquired immune deficiency retroviruses.

Applicants further note that in U.S. '208, the muramyl peptides were only administered to healthy patients, i.e. not patients in need of inhibition of retrovirus replication, as recited in the present claims and with U.S. '208 the muramyl peptide was never exposed to HIV virus. Thus, the claims of U.S. '208 do not explicitly or inherently teach or suggest the presently claimed method of the present invention or render the present invention obvious. Withdrawal of the rejection is, therefore, respectfully requested.

Rejections under 35 U.S.C.§112, 1st paragraph

Claims 25, 26 and 28-34 have been rejected under 35 U.S.C.§112, 1st paragraph, with the assertion that recitation of "as a principal ingredient" is new matter. Applicants traverse this rejection and withdrawal thereof is respectfully requested.

As noted by the Examiner, the specification need not provide *in haec verba* support for the language added to a claim. A determination of whether a feature added to the claim is adequately supported by the specification, so as to not be new matter was

discussed in All Dental Prodx, LLC v. Advantage Dental Prods., Inc., 309 F.3d 774, 64 U.S.P.Q.2d (BNA) 1945 (Fed. Cir. 2002), wherein the Court of Appeals for the Federal Circuit held that,

> the failure of the specification to specifically mention a limitation that later appears in the claims is not a fatal one when one skilled in the art would recognize upon reading the specification that the new language reflects what the specification shows has been invented.

Thus, the proper determination of whether recitation in the claims that the muramyl peptide is administered "as a principal ingredient" is new matter turns on whether one skilled in the art would have recognized this feature as part of the invention. The specification on page 7 recites,

> The molecules of the invention may be used in human clinical medicine either for preventative purposes in seropositive individuals before the appearance of clinical signs or in patients having developed manifestations of AIDS. The therapeutic doses of the muramyl peptide (for example, Murabutide or Murametide) to be administered either alone, or in combination with antiviral treatments, particularly cytokines are between 1μg and 500μg/kg/day. (emphasis added)

From the last sentence, particularly recitation that the muramyl peptides may be administered alone, it is unequivocally clear from the specification that the invention regards the administration of the muramyl peptide as the main ingredient, i.e. principle ingredient, for the inhibition of acquired immunodeficiency retroviruses in man or susceptible animals.

Further support is found from the overall teachings of the specification, which wholly discuss the ability of muramyl peptides, alone, to cause the 100% inhibition of retrovirus replication. In addition, all of the experiments test and demonstrate the inhibitory properties of muramyl peptides. For example, page 6 final paragraph, demonstrates the ability of murmayl peptides, alone, to inhibit HIV replication in primary cultures of human monocytes. The experimental results of the experiments are shown in Table 2 and demonstrate complete inhibition of retrovirus replication with treatment at day (-1), day (0) or day (+1).

Thus, "one skilled in the art would recognize upon reading the specification that the new language ["as a principle ingredient"] reflects what the specification shows has been invented." As such, recitation of "as a principle ingredient" is not new matter and withdrawal of the rejection is respectfully requested.

Rejections under 35 U.S.C.§102(b)

(1) *Schreck et al.* - Claims 25, 26, 28-30 and 34 have been rejected under 35 U.S.C.§102(b) as being anticipated by Schreck et al.

(2) *Masihi et al.* - Claims 25, 26, 28-30 and 34 have been rejected under 35 U.S.C. §102(b) as being anticipated by Masihi et al. The Examiner asserts that Masihi et al. teach the claimed invention with the teaching that murabutide increased the number of granulocyte-macrophage progenitors in mouse spleens.

These rejections are addressed individually and jointly in the Remarks that follow.

On page 5 of the office action, the Examiner presents the following assertions regarding Schreck et al.

a) The Examiner asserts that Schreck et al. refer to "murabutide" as an immunostimulant.

b) The Examiner also asserts that the reference to murabutide as an adjuvant is "a matter of semantics, since the term does not exclude other descriptive terms."

c) The Examiner asserts that the recited steps of the invention are the same steps disclosed in Schreck et al.

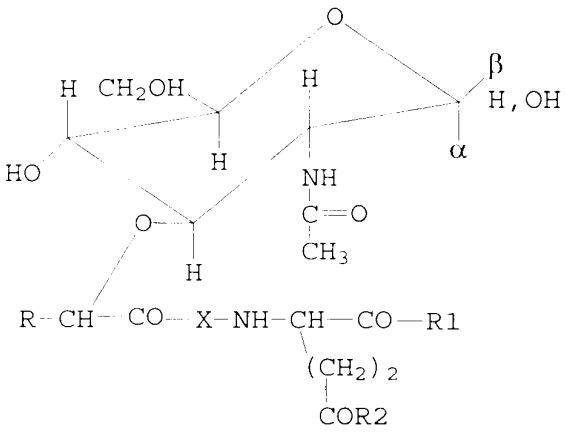
Applicants traverse this rejection and withdrawal thereof is respectfully requested. With regard to points a) and b), above, Applicants respectfully note that use of the terms "immunostimulant" versus "adjuvant" is not merely a matter of semantics. The Examiner may be correct if Applicants were claiming the muramyl compounds per se. In that case, whether a compound is

descriptively called an "immunostimulant" "an adjuvant" or is labeled by its chemical name, "muramyl peptide", would not matter for purposes of patentabililty. However, Applicants are not claiming the compounds but rather a method. As such, whether something is acting as an immunostimulant or an adjuvant is not merely a matter of semantics, i.e. the same thing with different names, but a defining feature of the method.

In this regard, it flows that the Examiner is incorrect with regard to the assertion of point c), i.e. that the recited steps of the invention are the same steps disclosed in Schreck et al.

"To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently." In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997).

The present invention of claims 25, 28-29 and 34 is drawn to a process for inhibiting the replication of acquired immunodeficiency retroviruses, by administering as a principal ingredient an effective amount of a muramyl peptide of formula:



wherein the effective amount is also an amount that is capable of causing a 100% inhibition of the replication of said retroviruses in primary cultures of monocytes of the host.

There is no disclosure or suggestion in Schreck et al. of inhibiting the replication of immundeficiency retroviruses with muramyl peptides. Rather, Schreck et al. teach the use of muramyl peptides as adjuvants in AIDS vaccines. Throughout the experimental section of this publication no HIV-1 infected cells were used. Rather three types of cells lines were used which were human Jurket T cells, a human monocyte-macrophage cell line called Mono-Mac-8 and a mouse pre-B cell line 70Z/3.12. As indicated in the Material and Methods section, none of these cell lines were infected with HIV-1. Thus, with Schreck et al. the compounds were

never exposed to HIV-1 and it was not possible to achieve the invention with Schreck et al., either explicitly or inherently.

The above arguments regarding Schreck et al. are similarly applicable to Masihi et al. Misihi et al. also teach the use of a muramyl peptide (murabutide) as an adjuvant. While there is a single sentence in Masihi et al. that murabutide was used as an adjuvant in human clinical trials for AIDS, there is no disclosure or suggestion that the murabutide itself had any effect on replication of retroviruses.

As discussed previously, an adjuvant cannot be considered as a principal ingredient in a vaccine, since it is the antigen *per se* that is foremost in importance in a vaccine to obtain immunity and not the adjuvant. It should be emphasized that importance is not a measure of quantity but effect.

Moreover, like Schreck et al., Masihi et al. is completely silent with respect to the results obtained from the AIDS trial. The mere statement that murabutide has been administered to a human does not imply that it has been used with success, such that HIV-1 replication was inhibited. It cannot be assumed or inferred from this sole sentence in Masihi et al. that inhibition of immunodeficiency retrovirus replication was in fact achieved.

The Supreme Court clearly stated in Eibel v Minnesota & Ontario Paper Co., "accidental results, not intended and not appreciated, do not constitute anticipation." Eibel Processing Co. v. Minnesota & Ontario Paper Co. 261 U.S. 45 (1923). The Federal Circuit stated in In re Roberton that, "to establish inherency...extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference *and it would be so recognized by persons of ordinary skill.*" (emphasis added) In re Roberston 49 U.S.P.Q.2d 1949 (Fed. Cir. 1999) similarly in Rosco v. Mirror Lite, the Federal Circuit held that for anticipation by inherency one skilled in the art must "read" the reference as disclosing the invention. Rosco v. Mirror Lite Co., 64 USPQ2d 1676 (Fed. Cir. 2002).

There is no way that one skilled in the art would ever read the one sentence disclosure in Masihi et al. that MDP was used as an adjuvant as inherently disclosing that an effective amount of the muramyl peptide was administered to a patient to inhibit the replication of immunodeficiency virus and that the amount of muramyl peptide administered was sufficient to result in 100% inhibition of HIV in primary cultures of monocytes of the host. As such, the threshold and showing for a rejection by inherency has not been met.

With regard to both Schreck et al. and Masihi et al. the Examiner asserts that the present invention encompasses the treatment of non-infected cells because "well settled patent law establishes that the preamble is not given patentable weight. Thus, there is no requirement for inhibition of the AIDS virus replication, and there is no requirement for virally infected cells prior to treatment."

However, the Examiner has both misinterpreted the claims and is legally incorrect in her position. As discussed below, the preamble is a limitation of the present claims. In addition, the disclosure of administering muramyl peptides to the culture of cells cannot be interpreted as being an inherent disclosure of prophylaxis, since as also noted below, a culture dish is not a man or animal and the present invention recites administering a "man or animal."

The Examiner's position is legally incorrect in the statement, "well settled patent law establishes that the preamble is not given patentable weight". Applicants note in this regard that the Examiner has not cited any case law in support of her position. The courts early on stated that "there is no general rule for deciding the weight given to claim preambles as positive structural recitations", In re Neugebauer et al., 51 CCPA 1138, 330 F.2d 353

(Ct. of Cust. & Pat. Apps.) 1964. The legal issue of whether the preamble is a limitation of the invention, i.e. has patentable weight, has been addressed as recently as this year (2003). In Eaton Corp. v. Rockwell Int'l Corp., 323 F.3d 1332, 66 U.S.P.Q.2d (BNA) 1271 (Fed. Cir. 2003), the Court of Appeals for the Federal Circuit presented a thorough review of case law regarding preambles and stated the following.

> In general, a preamble limits the [claimed] invention if it recites essential structure or steps, or if it is 'necessary to give life, meaning, and vitality' to the claim." Catalina Mktg. Int'l, Inc. v. Coolsavings.com, Inc., 289 F.3d 801, 808, 62 USPQ2d 1781, 1784 (Fed. Cir. 2002) (quoting Pitney Bowes, Inc. v. Hewlett-Packard Co., 182 F.3d 1298, 1305, 51 USPQ2d 1161, 1165 (Fed. Cir. 1999)). "[A] claim preamble has the import that the claim as a whole suggests for it. In other words, when the claim drafter chooses to use both the preamble and the body to define the subject matter of the claimed invention, the invention so defined, and not some other, is the one the patent protects." Bell Communications Research, Inc. v. Vitalink Communications Corp., 55 F.3d 615, 620, 34 USPQ2d 1816, 1820 (Fed. Cir. 1995). When limitations in the body of the claim rely upon and derive antecedent basis from the preamble, then the preamble may act as a necessary component of the claimed invention. See, e.g., Electro Sci. Indus. v. Dynamic Details, Inc., 307 F.3d 1343, 1348, 64 USPQ2d 1781, 1783 (Fed. Cir. 2002); Rapoport v. Dement, 254 F.3d 1053, 1059, 59 USPQ2d 1215, 1219 (Fed. Cir. 2001); Pitney Bowes, 182 F.3d at 1306, 51 USPQ2d at 1166. On the other hand, "[i]f the body of the claim sets out the complete invention," then the language of the preamble may be superfluous. Schumer v. Lab. Computer Sys., Inc., 308 F.3d 1304, 1310, 64 USPQ2d 1832, 1837 (Fed. Cir. 2002); Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc., 246 F.3d 1368, 1373-74, 58 USPQ2d 1508, 1512 (Fed. Cir. 2001).

Thus, whether the preamble is a patentable feature of the invention must be determined on a case-by-case basis and there is no set arbitrary rule from the case law as stated by the Examiner. The present claims recite several features in the preamble, which are clearly needed to "breathe life and meaning into the claims" and therefore are features of the invention. Firstly, the preamble recites "a method for inhibiting the replication of acquired immunodeficiency retroviruses in man or in...animals." Clearly a petri dish is not a man or animal. In addition, one skilled in the art would not be inhibiting the replication of acquired immunodeficiency retroviruses unless the retrovirus was present.

The claims further recite "which comprises administering as a principal ingredient to **said man or said animals in need of such treatment**..." The preamble provides antecedent basis for the underlined feature of the claim. "When limitations in the body of the claim rely upon and derive antecedent basis from the preamble, then the preamble may act as a necessary component of the claimed invention." Eaton Corp. v. Rockwell Int'l Corp., 323 F.3d 1332, 66 U.S.P.Q.2d (BNA) 1271 (Fed. Cir. 2003). Thus, the preamble, which provides antecedent basis must be considered a patentable feature of the invention.

The present invention is therefore novel and unobvious over Schreck et al. and Masihi et al. and withdrawal of the rejections is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, Ph.D. (Reg. No. 40,069) at the telephone number of the undersigned below.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____
Gerald M. Murphy, Jr., #28,977

MaryAnne Armstrong, PhD, #40,069

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

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